REMARKS

Applicants respectfully request reconsideration of the application, as amended, in view of the following remarks.

The present invention relates to methods in which an ophthalmic composition comprising from about **0.01% to about 0.1% of FK506** is administered to a patient.

The present invention as set forth in **amended Claim 1** relates to a method for treating a human patient suffering from dry eye, wherein prior to treatment said patient has a Schirmer score of less than or equal to seven millimeters per five minutes.

In **amended Claim 15**, the patient has prior to treatment a superficial punctate keratitis (SPK) score of at least two.

Amended Claim 16 relates to a method of treating a human patient suffering from an ocular surface damage associated with dry eye wherein prior to treatment the patient has a superficial punctate keratitis (SPK) score of at least two.

Amended Claim 17 relates to a method of treating a human patient suffering from an ocular discomfort associated with dry eye, wherein prior to treatment the patient has a Schirmer score of less than or equal to seven millimeters per five minutes.

Amended Claim 18 relates to a method of treating a human patient suffering from an ocular discomfort associated with dry eye, wherein prior to treatment the patient has a superficial punctate keratitis (SPK) score of at least two.

Amended Claim 19 relates to a method of treating a human patient suffering from an ocular surface damage associated with dry eye, wherein prior to treatment the patient has a Schirmer score of less than or equal to seven millimeters per five minutes.

In contrast, WO 00/66122, Tsubota et al, and Peyman fail to disclose or suggest methods for treating dry eye, ocular discomfort and ocular damage as claimed in which an ophthalmic composition comprising from about 0.01% to about 0.1% of FK506 is

administered to a patient who, prior to treatment, has a Schirmer score of less than or equal to seven millimeters per five minutes, or a superficial punctate keratitis (SPK) score of at least two.

WO 00/66122 discloses that 0.01% and 0.1% FK506 eye drops have a tear film breakup time improving effect. However, this reference does not disclose or suggest treating a patient who, prior to treatment, has a Schirmer score of less than or equal to seven millimeters per five minutes, or a superficial punctate keratitis (SPK) score of at least two.

Peyman cannot cure the defects of WO 00/66122 because all that this reference discloses is that a patient suffering from dry eye disease may complain of superficial keratitis, or corneal perforation. Based on the disclosure of Peyman, one of ordinary skill in the art does not know that an ophthalmic composition comprising from about 0.01% to about 0.1% of FK506 is effective in treating a patient who, prior to treatment, has a Schirmer score of less than or equal to seven millimeters per five minutes, or a superficial punctate keratitis (SPK) score of at least two.

Tsubota et al disclose that cyclosporine A is effective for an immunotherapy of dry eye. However, cyclosporin A is not FK506 nor is it a macrolide compound.

Therefore, the rejection of Claims 1-14, 17 and 18 under 35 U.S.C. § 102(b) as anticipated by WO 00/66122, the rejection of Claims 1-4, 7, 17 and 18 under 35 U.S.C. § 102(b) as anticipated by Tsubota et al, the rejection of Claims 15, 16 and 19 under 35 U.S.C. § 103(a) as being unpatentable over WO 00/66122 and Peyman (US 6,489,335) are believed to be unsustainable as the present invention is neither anticipated nor obvious and withdrawal of these rejections is respectfully requested.

Regarding the provisional obviousness-type double patenting over Serial Nos. 10/354,083 and 09/926,411 Applicants wish to draw the Examiner's attention to the MPEP which instructs the Examiner to withdraw the provisional rejection if it is the only issue

remaining in one case and convert the provisional rejection in the other application to a double patenting rejection. MPEP 822.01.

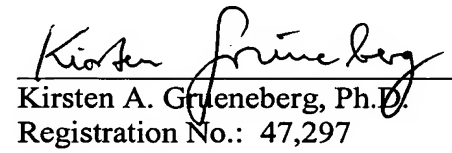
The rejection of Claims 1-19 are rejected under 35 U.S.C. §112, first paragraph, is obviated by the amendment of the Claims.

Applicants respectfully request that the Examiner acknowledge that the references cited in the **Information Disclosure Statement, filed** in the above-identified application on **August 23, 2004,** have been considered. For the Examiner's convenience a copy of Form PTO 1449 as filed on August 23, 2004, is attached herewith.

This application presents allowable subject matter, and the Examiner is kindly requested to pass it to issue. Should the Examiner have any questions regarding the claims or otherwise wish to discuss this case, he is kindly invited to contact Applicants' below-signed representative, who would be happy to provide any assistance deemed necessary in speeding this application to allowance.

Respectfully submitted,

OBLON, SPIVAK, McCLELLAND,
MAIER & NEUSTADT, P.C.
Norman F. Oblon



Kirsten A. Grueneberg, Ph.D.
Registration No.: 47,297

Customer Number
22850

Tel: (703) 413-3000
Fax: (703) 413 -2220
NFO:KAG: